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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/772,105	01/26/2001	Laurie J. Ozelius	0838.1001-009	7955

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[REDACTED] EXAMINER

EINSMANN, JULIET CAROLINE

[REDACTED] ART UNIT [REDACTED] PAPER NUMBER

1634

DATE MAILED: 08/14/2002

9

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/772,105	OZELIUS ET AL.
Examiner	Art Unit	
Juliet C Einsmann	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 24 May 2002.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-30 is/are pending in the application.
- 4a) Of the above claim(s) 3,5,7,9 and 13-27 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 2,4,6,8,10-12 and 28-30 is/are rejected.
- 7) Claim(s) 1,4,6,8,10,11 and 28-30 is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on 26 January 2001 is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some * c) None of:
1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>5</u> . | 6) <input type="checkbox"/> Other: _____. |

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I in Paper No. 8 is acknowledged.
2. Elected group I is drawn to nucleic acids that are fragments of the DYT1 gene, SEQ ID NO: 30-39, 48-56, and 88-90. The restriction requirement inadvertently indicated that this group contains claims 1-13 and 28-30. However, claims 3, 5, 7, 9, and 13 do not recite nucleic acids that are fragments of the DYT1 gene. Thus, these claims are considered non-elected. Claims 1, 2, 4, 6, 8, 10, 11, and 12 are examined herein.

Priority

3. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

This application is claiming the benefit of a prior filed nonprovisional application under 35 U.S.C. 120, 121, or 365(c). Copendency between the current application and the prior application is required.

In the instant case, the claimed subject matter is first disclosed in application serial number 09/461921, which was abandoned 11/25/00. Thus, there is not copendency between the instant application and the earlier filed application. It is noted, for the record, however, that nucleic acids consisting of SEQ ID NO: 30-39, 48, 49, 50, 51, 53, 54, 55, 56, and 89 are first disclosed in the 09/461921 application. Nucleic acids comprising or consisting of instant SEQ ID NO: 52, 88, and 90 are first disclosed in the instant application.

Claim Objections

4. Claims 1, 10, 11, 28, 29, and 30 are objected to because they contain specific recitations of non-elected subject matter. Prior to allowance non-elected subject matter must be cancelled from the claims.
5. Claims 4, 6, and 8 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The claims are broader in scope than claim 2 from which they depend. That is, the claims does not require all of the limitations of the parent claim, and thus they are confusing.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.
7. Claims 4, 6, 8, and 30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 4, 6, and 8, are indefinite because they are broader in scope than claim 2 from which they depend. That is, the claims does not require all of the limitations of the parent claim, and thus they are confusing because it is not clear if they are meant to encompass all of the limitations of claim 2 from which they depend.

Claim 8 is further indefinite over the recitation "sequence of about 20 to 50 nucleic acids" because it is not clear if applicant intends for 20 to 50 different nucleic acids to be encompassed in the claim or a nucleic acid of 20 to 50 nucleotides.

Claim 30 is indefinite because reads "the method of claim 29" but it depends from a product claim. For the purposes of examination herein claim 30 has been treated as a product claim. If it is method claim, then claim 30 would have been restricted away (see paper number 6).

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 2, 4, 6, 8, 12, and 28-30 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 2, 4, 6, 8, and 12 are drawn to isolated nucleic acids that are defined as having a percent homology with one of SEQ ID NO: 30-39, 48-56, and 88-90. For each particular sequence, the large genus encompassed by the claims is represented in the specification by a single species, that is the particular sequence which is disclosed. Claims 28-30 are drawn to genes comprising mutations which result in a dopamine-mediated or neuronal disease. The instant specification only teaches one such gene and mutation that could be detected with the primers recited in claims 28-30, and this is the DYT1 gene encoding torsinA. Thus, for each of these broad claims, applicant has express possession of only one species in a genus which comprises hundreds of millions of different possibilities.

With regard to the written description, claims 2, 4, 6, 8, and 12 encompass nucleic acid sequences different from those disclosed in the specific SEQ ID No:s which, for claims 2, 4, 6, 8, and 12 include modifications by permitted by the % identity language for which no written description is provided in the specification. The specification does not contain any particular guidance as to how these sequences can be modified and still retain their function. Furthermore, it is noted for 4, 6, and 8 these claims encompass nucleic acids of unlimited length that are required to share as little as only 16 nucleotides in common with the parent sequence from which they are derived.

Claims 28-30 encompass an unknown number of genes from humans and other mammal genes that are structurally limited in the claim only by the fact that they have to contain an undefined mutation or polymorphism and be detectable using SEQ ID NO: 30-39. Outside of these two limitations the chemical structure of genes encompassed by claims 28-39 are structurally undefined.

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

"...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

In the instant application, only the nucleic acid sequences of the disclosed SEQ ID Nos are described. Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

"...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

The instantly disclosed SEQ ID NO: 30-39, 48-56, and 88-90 have their utility in the ability to detect the DYT1 gene which is associated with torsin dystonia. In the application at the time of filing, there is no record or description which would demonstrate conception of any proteins modified by addition, insertion, deletion, substitution or inversion with the disclosed sequences but possessing one or more nucleic acid differences such that a different nucleic acid sequence results which retains the function of the disclosed sequences.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

- (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
- (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 2 and 8 are rejected under 35 U.S.C. 102(a) as being anticipated by GenBank Record AL158207 (GI: 7160605).

The GenBank record provides an isolated nucleic acid molecule comprising a polynucleotide sequence at least 90% identical to a sequence selected from the group consisting of SEQ ID NO: 48-56 and 88-90. The nucleic acid provided in the GenBank record comprises isolated nucleic acids that are at least 90% identical to each of SEQ ID NO: 48, 49, 51, 52, 53, 54, 55, 56, 88, 89, and 90. For example, the sequence taught in the record comprises a polynucleotide with 100% local similarity to instant SEQ ID NO: 90 (nucleotides 74593-74792 are identical to SEQ ID NO: 90). As another example, the complement of nucleotides 85781-85405 of the GenBank record have 93.5% local similarity with instant SEQ ID NO: 88, as is

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exemplified in the following alignment. The alignment is of SEQ ID NO: 88 against the complement of the sequence found in the GenBank record. The sequence labeled "Qy" is SEQ ID NO: 88, and the sequence labeled Db is the complement of the sequence within the GenBank record.

```

Query Match           75.0%;  Score 283.6;
Best Local Similarity   93.5%;  Pred. No. 1.6e-71;
Matches    359;  Conservative    0;  Mismatches    12;  Indels    13;  Gaps
6;

Qy      1 ctggaaagacaaagccaatcaggagtggggaaagaaaca-cggcaaaatgttagccacatt 59
       ||||||| | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
Db     85781 CTGGGAAAGACAAAGCCAATCAGGAGTGGGGAAAGAACAGCGGAAAATGTAGCCACATT

Qy      60 tacagcccataaganagccagcaaagccgtctag----cctccaagcaccttgcgaaacc 115
       ||||||| | | | | | | | | | | | | | | | | | | | | | | | | | | | |
Db      TACAGCCCATAAGAAAGCCAGCAAAGCCGTCTAGACGCCCTCCAAGCACCTTGCAGAAACC

Qy      116 tcaagtactgcggctgttaagctcctggccagagggacggcggtccagggngccctc 175
       ||||||| | | | | | | | | | | | | | | | | | | | | | | | | | | | |
Db      TCAAGTACTGCGGTCT-GTAAGCTCCTGGCCAGAGGGACGGCGGTCCAGGGAGCCCTC

Qy      176 ccttgctggcctgcctattctaaagccctggccgnctcattccggaaaagccccttg 235
       ||||||| | | | | | | | | | | | | | | | | | | | | | | | | | | |
Db      CCTTTGCTGGCCTGCCTATTCTAAAGCCCTGGCCGACTCCTCCGAAAAGCCCCTTG

Qy      236 gtgccactgccactgccaccanttgcnccccct-acccctgtntctgtcctcccaaaaa 294
       ||||||| | | | | | | | | | | | | | | | | | | | | | | | | | |
Db      GTGCCACTGCCACTGCCACCAGTTGCACCCCTAACCCCTGTGCTGCTCCTCCCACCCCA

Qy      295 aggcatgcggnnngnagaaggaaacanttggcccttcgtcgctcgnggaagac 354
       ||||| | | | | | | | | | | | | | | | | | | | | | | | | | | | |
Db      AGGCAGAGCCGG-----GAAAGGAAACAGTTGGTCCCTCCTGGTCGGCT-GCGGAAGAG

Qy      355 tcctcaccatccatcctgtcttcc 378
       ||||||| | | | | | | | | | | | | | | | | | | | | | | |
Db      TCCTCACCATCCTTCCTGTCTCCC 85405

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Additional alignments have not been included because they would be duplicative since the claim only requires the presence of an isolated nucleic acid comprising a polynucleotide sequence at least 90% identical to one of SEQ ID NO: 48-56 and 88-90.

Claim 10 is also rejected because the nucleic acid taught in the GenBank record comprises a polynucleotide molecule of 20 to 50 nucleic acids which is at least 80% identical to a sequence according to claim 2. For example, the GenBank record teaches a nucleic acid that comprises a polynucleotide that is 100% identical to nucleotides 1-50 of instant SEQ ID NO: 90.

It is noted that this reference is a 102(a) type reference against these claims because priority was not granted in this application to 09/461921 because there was no copendency between the '921 application and the instant application. However, even if there were copendency between the two applications, these claims would not have been entitled to the earlier priority date because they recite nucleic acid sequences that were not recited in the earlier application. Thus, the claim would have been entitled to only the benefit of the instant filing date (i.e. nucleic acids consisting of SEQ ID NO: 52, 88, and 90).

12. Claims 2, 8, and 28-30 are rejected under 35 U.S.C. 102(b) as being anticipated by Ozelius et al. (Nature Genetics, Volume 17, 1997, pages 40-48).

Ozelius et al. teach provides an isolated nucleic acid molecule comprising a polynucleotide sequence at least 90% identical to a sequence selected from the group consisting of SEQ ID NO: 48-56 and 88-90 (Figure 1). Instant SEQ ID NO: 48-56 and 88-90 are nucleic acids that cDNA clones of DYT1 gene introns. DYT1 is the gene encoding torsinA, and is referred to in the paper by Ozelius et al. as DQ2. Ozelius et al. teach a series of cosmid contigs that are isolated nucleic acids containing genomic DNA from human chromosome 9q, and cosmid 29A5 is the cosmid that would contain the genomic DNA from which DQ2 is transcribed. Thus, Cosmid 29A5 LA taught by Ozelius et al. would comprise the introns of the DQ2 gene and is therefore is an isolated nucleic acid molecule that inherently comprises a

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polynucleotide sequence at least 90% identical to a sequence selected from the group consisting of SEQ ID NO: 48-56 and 88-90. Although Ozelius et al. does not disclose the sequence of this cosmid, the cosmid taught by Ozelius et al. appears to be substantially identical to the nucleic acid claimed in claim 2.

Furthermore, Ozelius et al. teach an isolated nucleic acid molecule comprising a polynucleotide sequence of about 20 to 50 nucleotides which is at least 80% identical to a sequence according to claim 2. For example, Ozelius et al. teach a nucleic acid that comprises a polynucleotide that is 100% identical to nucleotides 1-50 of instant SEQ ID NO: 89 (see alignment below. The line labeled Qy is instant SEQ ID NO: 89. The line labeled Db is the sequence of DQ2 as disclosed in GenBank AF007871 (p. 47, Ozelius et al.)).

```
Query Match           14.7%;  Score 59;  DB 9;  Length 2072;
Best Local Similarity 100.0%;  Pred. No. 1.2e-20;
Matches      59;  Conservative     0;  Mismatches     0;  Indels      0;  Gaps
0;

Qy      1 gaatatttacgagggtggctgaacagtgactatgtccacctgtttgtggcacattgc 59
        ||||||| ||||||| ||||||| ||||||| ||||||| ||||||| ||||||| ||||||| |||||
Db      393 GAATATTTACGAGGGTGGCTGAACAGTGACTATGTCCACCTGTTGTGGCACATTGC 451
```

With regard to claims 28-30, Ozelius et al. teach a gene comprising a gene mutation resulting in a dopamine-mediated disease in a mammal and could be detected by the method recited in the claims (see, for example Figure 5 and the DQ2 gene). Ozelius et al. teach that the sequence of the DQ2 gene is disclosed in GenBank AF007871 (p. 47). This sequence comprises instant SEQ ID NO: 31, 32, and 39, and thus could be detected by any one of these primers.

13. Claims 4 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Ozelius et al. (WO 98/57984).

Ozelius et al. teach an isolated nucleic acid molecule consisting of twenty or forty consecutive nucleotides from a nucleotide sequence comprising a polynucleotide sequence at

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least 90% identical to a sequence selected from the group consisting of SEQ ID NO: 48-56 and 88-90 (p. 25). Specifically, Ozelius et al. teach probes that consist of nucleotides 43-62 or 43-82 of their SEQ ID NO: 5. These probes are contained within the GenBank record that is cited previously against claim 2 (see nucleotides 84542-84582 of the GenBank record). Thus, the probes taught by Ozelius et al. isolated nucleic acid molecules consisting of 20 and 40 consecutive nucleotides from a nucleotide sequence according to claim 2.

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

15. Claims 6, 10, 11, and 12 rejected under 35 U.S.C. 103(a) as being unpatentable over Ozelius et al. (WO 98/57984).

With regard to claim 6, Ozelius et al. teach an isolated nucleic acid molecule consisting of twenty or forty consecutive nucleotides from a nucleotide sequence comprising a polynucleotide sequence at least 90% identical to a sequence selected from the group consisting of SEQ ID NO: 48-56 and 88-90 (p. 25). Specifically, Ozelius et al. teach probes that consist of nucleotides 43-62 or 43-82 of their SEQ ID NO: 5. These probes are contained within the GenBank record that is cited previously against claim 2 (see nucleotides 84542-84582 of the GenBank record). Thus, the probes taught by Ozelius et al. isolated nucleic acid molecules consisting of 20 and 40 consecutive nucleotides from a nucleotide sequence according to claim 2.

Ozelius et al. teach an isolated nucleic acid which comprises instant SEQ ID NO: 31, 32, and 39 (see SEQ ID NO: 5). The complement of nucleotides 153-172 of SEQ ID NO: 5 in Ozelius et al. are identical to instant SEQ ID NO: 31. Nucleotides 162-181 of SEQ ID NO: 5 in Ozelius et al. are identical to SEQ ID NO: 32. The complement of nucleotides 1295-1213 of SEQ ID NO: 5 in Ozelius et al. are identical to instant SEQ ID NO: 39.

Furthermore, Ozelius et al. teach that a preferred embodiment of their invention includes nucleic acid probes for the specific detection of the presence of torsin nucleic acid in a sample (p. 24, lines 18-21), that such nucleic acids should be or be complementary to 10 consecutive nucleotides (p. 24, lines 27-28), and they provide specific examples of such probes from their SEQ ID NO: 5 (p. 25). Ozelius et al. teach that one skilled in the art can readily design such probes based on the sequences that they disclose using methods of computer alignment and sequence analysis known in the art (p. 26, lines 14-18).

Ozelius et al. do not teach nucleic acid molecules consisting of SEQ ID NO: 31, 32, or 39. However, given the specific guidance provided by Ozelius et al. and the suggestion by Ozelius et al. to select probes from within and complementary to their SEQ ID NO: 5, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have selected additional probes from within the sequences taught by Ozelius et al. The ordinary practitioner would have been motivated to select such probes “for the specific detection of the presence of torsin nucleic acid in a sample (p. 24)” as taught by Ozelius et al. Although the probes of the instant invention are not specifically taught by Ozelius et al., they are considered functional homologues of the probes taught by Ozelius et al. in that they would be able to detect torsin nucleic acids in a sample, and as such, they are considered *prima facie*

obvious in view of the prior art. Furthermore, in light of the teachings of Ozelius et al., it would have been *prima facie* obvious to have made the complement of any of the exemplified probes taught by Ozelius et al. in order to have provided additional probes for the detection of torsin nucleic acids.

Conclusion

16. No claims are allowed. Claim 1 would be allowable if the non-elected sequences were removed from the claim. The prior art does not teach or suggest isolated nucleic acids consisting of instant SEQ ID NO: 48-56 or 88-90. The closest prior art is cited of record, and although this prior art teaches nucleic acids comprising one or more of these sequences, the prior art does not specifically teach or suggest isolated nucleic acids that consist of these intronic sequences. Thus, the claim is free of the prior art with regard to the elected sequences.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C. Einsmann whose telephone number is (703) 306-5824. The examiner can normally be reached on Monday through Friday, from 9:00 AM until 4:00 PM.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 and (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



Juliet C. Einsmann
Examiner
Art Unit 1634

August 9, 2002



W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600